



Open or Endovascular Repair of Aortoenteric Fistulas? A Multicentre Comparative Study **CME**

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KEYWORDS

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Abstract *Objectives:* To compare aortoenteric fistula (AEF) outcome after endovascular (EV-AEFR) or open repair (O-AEFR).

Design: Multicentre retrospective comparative study.

Materials/Methods: 25 patients with AEF (24 secondary, 23 males, median age 75 years) after aortic surgery (median four years). Preoperative sepsis was evident in 19 cases. Eight patients were managed with EV-AEFR and 17 with O-AEFR.

Results: The two groups were comparable in preoperative characteristics. In-hospital mortality after EV-AEFR was lower compared to O-AEFR (0% and 35%, respectively, $p = 0.13$). Similarly, morbidity after EV-AEFR was lower compared to O-AEFR (25% and 77%, respectively, $p = 0.028$). There was a trend for worse recurrence-free, sepsis-free, re-operation-free and AEF-related death-free rates after EV-AEFR, while the early survival advantage of EV-AEFR was lost after two years and the overall long-term survival rates (perioperative mortality included) of the two groups were similar. Preoperative sepsis had no effect on recurrence and sepsis-free rates ($p = 0.94$ and $p = 0.92$, respectively), but it was associated with worse two year overall survival (24% vs 50%, $p = 0.32$). On multivariate analysis, the number of symptoms (two vs one) at presentation was the single predictor of worse re-operation rates, AEF-related and overall survival.

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Conclusions: EV-AEFR was associated with no postoperative mortality in this study and can achieve satisfactory short and long-term results, comparable to O-AEFR. Further trials should focus on the role of EV-AEFR in patients at high risk for O-AEFR, due to shock or co-morbidities, or as a bridging procedure.

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Despite prompt open surgery, aortoenteric fistula (AEF), mostly secondary after abdominal aortic aneurysm (AAA) repair, remains a highly lethal condition, with mortality rates of approximately 50%.¹ Although these rates seem to have decreased over time,¹ the prognosis is still dismal, especially in the presence of co-morbidities, risk factors such as advanced age or severe complications, such as haemorrhagic shock and sepsis. These observations call for a less invasive treatment modality. During the past decade, endovascular AEF repair (EV-AEFR) has emerged as a less morbid approach,^{2–7} despite the fact that its exact role as a definite or bridge treatment has to be defined, the latter being suggested because of a high incidence of recurrent bleeding and sepsis.⁸ Meta-analyses of case series of either method might be less valid than a direct comparison; so far, there is only one such study comparing EV-AEFR with open AEF repair (O-AEFR), but because it is small, any conclusions drawn from it need to be validated.⁶

The aim of our study was to compare short and long-term outcome after EV-AEFR or O-AEFR, to help the decision-making process of patient care.

Material and Methods

During a 12-year period (1998–2009), 25 patients with AEF (24 secondary, 23 males, median age 75 years) were operated on in six Greek Vascular Surgery Departments. Data were retrospectively collected in this multicentre comparative study; patients were divided in two groups, EV-AEFR and O-AEFR. Local expertise, surgeon preference and availability of the appropriate endograft influenced the decision-making process. Eight patients were managed with EV-AEFR and 17 with O-AEFR. Details of some patients in the EV-AEFR group have been partially provided in published case reports.^{7,9,10} AEFs occurred after a median of 4 years after aortic surgery (endovascular aneurysm repair (EVAR) in four cases), while preoperative sepsis was evident in 19 cases (76%, with fever in 14, (56%)).

Statistics

All data were analysed with Statistical Package for Social Sciences (SPSS) 17 or PASW statistics 18 (SPSS Inc., Chicago, IL, USA). Because of the small sample size, non-parametric tests were used. Categorical data were analysed with chi-square or Fisher's exact test, where appropriate. Event rates during follow-up included recurrence, sepsis, combined recurrence and sepsis, re-operation, AEF-related death and overall survival; these were evaluated and graphically depicted with the Kaplan–Meier curve methodology, while the log-rank test was used to compare the event rates among the various subgroups. To increase the power of the study, postoperative events were included, with the exception of tests studying the effect of

antibiotics prescribed at discharge. Cox proportional-hazard models were used for multivariate analysis.

Results

Patient demographics in relation to study group are shown in Table 1. The two study groups were comparable in terms of preoperative characteristics. Patient symptoms and preoperative investigations are shown in Table 2. There was a trend for preoperative sepsis being less common in the EV-AEFR group compared with the O-AEFR group. Further, computed tomography (CT) findings of periprosthetic inflammation, air or pseudo-aneurysm formation in the EV-AEFR group (100%, 38% and 38%, respectively) and the O-AEFR group (81%, 94% and 6%, respectively) were not significantly different ($p = 1.00$, $p = 0.07$ and $p = 0.09$, respectively). One patient in the O-AEFR group had a periprosthetic abscess formation. Periprosthetic air was observed more often in patients with preoperative fever (86%), raised inflammatory markers (92%) and sepsis (83%) compared with those without these clinical presentations (40%, $p = 0.032$, 36%, $p = 0.008$, 17%, $p = 0.007$, respectively).

Participating institutions managed between 1 and 8 cases. Five institutions performed at least one EV-AEFR, and all institutions performed O-AEFR. EV-AEFR was performed in 36% (4/11) of all cases performed through 2007 inclusive and in 29% in more recent cases ($p = 1.00$, Fisher's exact test). Operative findings and procedures performed in the EV-AEFR and O-AEFR groups are shown in Table 3. AEF variety and location (duodenum in 80%) were similar between the two study groups. A variety of endovascular procedures were performed, with placement of aortic cuff extenders being more common, followed by aortouniiliac endografting and femoro–femoral bypass. In the O-AEFR group, graft removal, closure of the aortic stump and intestine and axillobifemoral bypass grafting (delayed in one patient) were performed in 12 (71%) patients. In the remaining five patients (two of them with a paraprosthetic AEF/graft-enteric erosion), the graft was not removed; this was due to the fact that in one of them the AEF was primary (as a result of a psoas abscess and the aortic defect was sutured), in three of them it was an endograft for AAA repair and in the last the AEF was caused by a proximal anastomotic pseudo-aneurysm, which was repaired with *in situ* graft placement. Simple intestinal repair was performed in half of O-AEFRs, with complex repair (resection or duodenal closure and restoration of the intestinal continuity) being performed in the remainder. All patients received broad-spectrum antibiotics started preoperatively and continued throughout patient discharge. Median (interquartile) number of antibiotics in the EV-AEFR and O-AEFR groups was 2 (2–3) and 2 (2–3), respectively ($p = 0.54$) (information not available for three patients, two of them in the O-AEFR group).

Table 1 Patient baseline characteristics and pertinent history in the two study groups. Numerical data are expressed as median (interquartile range).

| Characteristic | Group | | <i>p</i> value | All patients (<i>n</i> = 25) |
|--|-------------------------|-------------------------|----------------|-------------------------------|
| | EV-AEFR (<i>n</i> = 8) | O-AEFR (<i>n</i> = 17) | | |
| Age (years) | 75.5 (71–78) | 73.5 (59–80) | 0.66 | 75 (60.5–79.5) |
| Gender (M/F) | 8/0 | 15/2 | 1.00 | 23/2 |
| AEF type (secondary/primary) | 8/0 | 16/1 | 1.00 | 24/1 |
| <i>Indication for primary operation</i> | | | | |
| AAA | 5 (63%) | 10 (63%) | 1.00 | 15 (63%) |
| AIOD | 3 (37%) | 6 (37%) | | 16 (37%) |
| <i>Type of primary operation</i> | | | | |
| Open repair or bypass grafting | 8 (100%) | 12 (75%) | 0.26 | 20 (83%) |
| Endovascular repair | 0 (0%) | 4 (25%) | | 4 (17%) |
| Time since original aortic surgery (years) | 4 (1–7.5) | 3.5 (1–8.8) | 0.85 | 4 (1.1–7.5) |

AAA: abdominal aortic aneurysm, AIOD: aortoiliac occlusive disease.

Short-term outcome

Postoperative complications are shown in Table 4. Morbidity after EV-AEFR was lower compared with O-AEFR (25% and 77%, respectively, $p = 0.028$, odds ratio 98, 95% confidence interval (C.I.) 1.4–69). Morbidity was higher in patients with periprosthetic air (86%) compared with those without air (25%, $p = 0.032$, odds ratio 9, 95% C.I. 1.3–64). Similarly, morbidity was higher in patients with perioperative sepsis or raised inflammatory markers (74% and 86%, respectively) compared with those without these characteristics (17%, $p = 0.023$, odds ratio 14, C.I. 1.3–151 and 27%, $p = 0.005$, odds ratio 16, C.I. 2.2–118, respectively). No other associations were identified. In-hospital mortality after EV-AEFR and O-AEFR was 0% and 35%, respectively ($p = 0.13$). Causes of death included multiple organ failure ($n = 4$), sepsis ($n = 1$) and intra-operative arrest and death

($n = 1$). Postoperative hospitalisation (median and interquartile range) in the EV-AEFR and O-AEFR groups was 10 (8–29) days and 21 (8–36) days, respectively ($p = 0.48$). Intensive care unit (ICU) stay (median and interquartile range) in the EV-AEFR and O-AEFR groups was 1 (0–3) days and 2 (0.5–8) days, respectively ($p = 0.19$). Patients, who had O-AEFR and their graft was not removed during this index operation ($n = 4$), had higher mortality (75%) compared with the remaining patients of both groups (14%, $p = 0.03$, odds ratio 18, 95% C.I. 1.4–236). Mortality in patients with preoperative sepsis was 32%, compared with 0% in those without sepsis ($p = 0.28$). Further, mortality in patients of the O-AEFR group, who had duodenal closure and gastric diversion, was 20%, compared with 33% in those who had simple primary repair and 67% in whom resection with primary anastomosis was performed ($p = 0.40$). Postoperative mortality was not associated with any other

Table 2 Patient symptoms and preoperative investigations in the endovascular and open groups.

| Characteristic | Group | | <i>p</i> value | All patients (<i>n</i> = 25) |
|--|-------------------------|-------------------------|----------------|-------------------------------|
| | EV-AEFR (<i>n</i> = 8) | O-AEFR (<i>n</i> = 17) | | |
| <i>Presenting symptom</i> | | | 0.49 | |
| Isolated GI bleeding | 4 (50%) ^a | 7(41%) | | 11 (44%) |
| Isolated fever | 0 (0%) | 3 (18%) ^a | | 3 (12%) |
| Combination of both | 4 (50%) | 7 (42%) | | 11 (44%) |
| Active hemorrhage | 3 (38%) | 5 (29%) | 1.00 | 8 (32%) |
| <i>Preoperative infection (n, %)</i> | 4 (50%) | 15 (88%) | 0.06 | 19 (76%) |
| Fever | 4 (50%) | 10 (59%) | 1.00 | 14 (56%) |
| Raised inflammatory markers ^b | 2 (25%) | 12 (71%) | 0.08 | 14 (56%) |
| <i>Preoperative investigations</i> | | | | |
| CTA | 8 (100%) | 16 (94%) | 1.00 | 24 (96%) |
| Oesophagogastroduodenoscopy | 7 (88%) | 10 (59%) | 0.21 | 17 (68%) |

^a One case with coexisting limb ischaemia.

^b White cell count ($>11,000/\text{mm}^3$), ESR ($>20 \text{ mm/h}$) or CRP ($>1 \text{ mg/dL}$).

Table 3 Operative findings and procedures performed in the endovascular and open groups. Intestinal involvement in the EV-AEFR group was mostly determined by preoperative investigations.

| Characteristic | Group | | <i>p</i> value | All patients (<i>n</i> = 25) |
|--|-------------------------|-------------------------|----------------|-------------------------------|
| | EV-AEFR (<i>n</i> = 8) | O-AEFR (<i>n</i> = 17) | | |
| <i>Intestine segment involved</i> | | | | |
| Duodenum | 6 (75%) | 14 (82%) | 1.00 | 20 (80%) |
| Jejunum or ileus | 2 (25%) | 3 (18%) | | 5 (20%) |
| <i>AEF variety</i> | | | | |
| Direct aortoenteric communication (anastomotic) | 8 (100%) | 14 (82%) | 0.53 | 22 (88%) |
| Paraprosthetic (graft-enteric erosion) | 0 (0%) | 3 (18%) | | 3 (12%) |
| <i>Endovascular procedures</i> | | | | |
| Aortouniliac endograft + femorofemoral bypass grafting | 3 (38%) | | | 3 (12%) |
| Aortic cuff extenders | 4 (50%) | | | 4 (16%) |
| Modular endograft | 1 (12%) | | | 1 (4%) |
| <i>Open procedures</i> | | | | |
| Graft removal + axillobifemoral bypass grafting | | 12 (71%) ^a | | 12 (48%) ^a |
| Graft left in place | | 4 (23%) | | 4 (23%) |
| Primary closure | | 1 (6%) | | 1 (6%) |
| <i>Intestinal repair</i> | | | | |
| Simple primary repair | 1 (13%) | 9 (53%) ^b | | 9 (36%) ^b |
| Resection with primary anastomosis | | 3 (18%) ^c | | 3 (12%) ^c |
| Duodenal closure + gastric diversion ^d | | 5 (29%) | | 6 (24%) |

^a Delayed axillofemoral bypass grafting in one patient.^b Hybrid repair in one patient.^c Aortic omentoplasty in one patient.^d Gastrojejunostomy (*n* = 3) or Roux-en-Y reconstruction (*n* = 2).

preoperative clinical characteristic or procedures performed. Median (interquartile) number of antibiotics taken after hospital discharge in the EV-AEFR and O-AEFR groups was 1 (1–2) and 1(0–1), respectively ($p = 0.034$) (information not available in three patients, two of them in the EV-AEFR group). Percentage of patients in the EV-AEFR and O-AEFR groups receiving antibiotics for more than 6 months was 67% and 20%, respectively ($p = 0.12$).

Long-term outcome

Regarding the main outcome measures of the study: recurrence-free, sepsis-free, combined event-free, re-operation-free, AEF-related death-free and overall long-term survival rates (perioperative mortality included), there was a trend for worse long-term results of the EV-AEFR patients, although the difference did not reach

Table 4 Complications and mortality in the endovascular and open groups.

| Complication | Group | | <i>p</i> value | Odds ratio (95% c.i.) | All patients (<i>n</i> = 25) |
|----------------------------|-------------------------|-------------------------|----------------|-----------------------|-------------------------------|
| | EV-AEFR (<i>n</i> = 8) | O-AEFR (<i>n</i> = 17) | | | |
| Multiple organ failure | 0 (0%) | 5 (29%) ^a | 0.140 | N/A | 5 (20%) |
| Bleeding | 0 (0%) | 2 (12%) ^b | 1.00 | N/A | 2 (12%) |
| Ischemic leg complications | 1 (13%) | 5 (29%) | 0.624 | 2.9 (0.28–30.3) | 6 (24%) |
| Limb loss | 1 (13%) | 2 (12%) | 1.00 | 0.93 (0.07–12.1) | 3 (12%) |
| Other complications | 1 (13%) ^c | 4 (24%) ^d | 1.00 | 2.1 (0.2–23.1) | 5 (20%) |
| Morbidity (total) | 2 (25%) ^e | 13 (77%) | 0.028 | 9.8 (1.4–69) | 15 (60%) |
| Mortality | 0 (0%) | 6 (35%) | 0.129 | N/A | 6 (24%) |

^a Gastrointestinal anastomosis leak in one patient.^b Recurrent bleeding in two patients (stump blowout in one of them), managed with simple suture and repeat infrarenal aortic stump ligation, initially, followed by recurrence and suprarenal ligation and splenorenal bypass, respectively.^c Respiratory failure and sepsis.^d MI, wound infection, gastrointestinal fistula, intra-operative arrest.^e Three additional patients with preoperative sepsis had postoperatively persistent sepsis (therefore not considered as a complication *per se*), managed successfully with antibiotics alone.

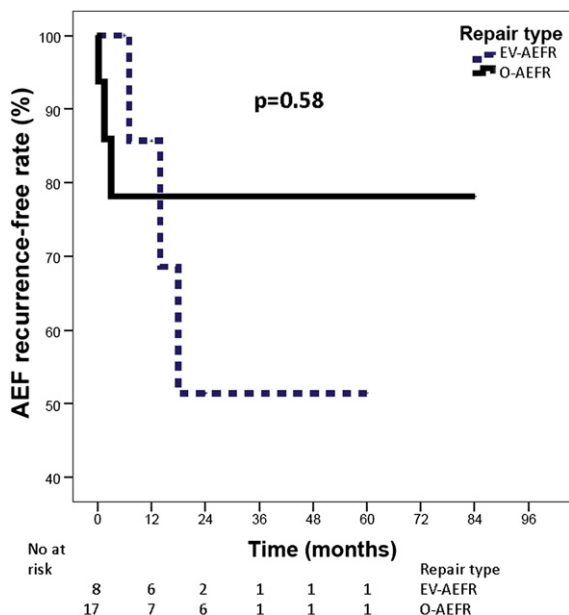
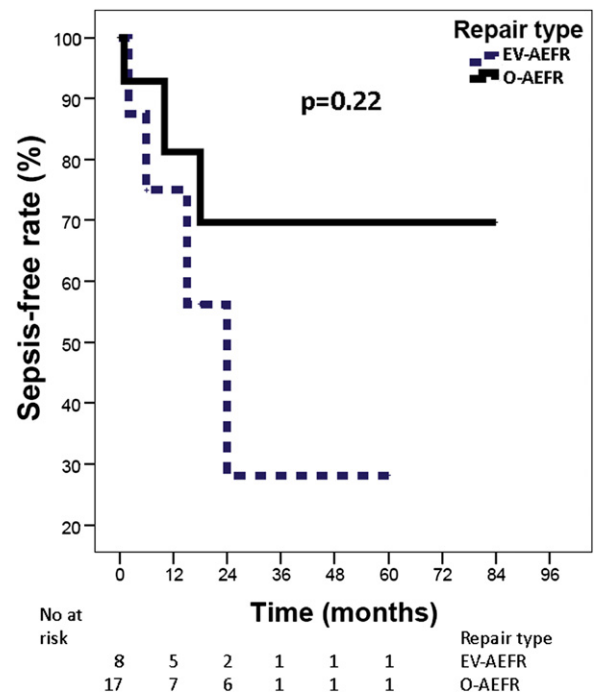
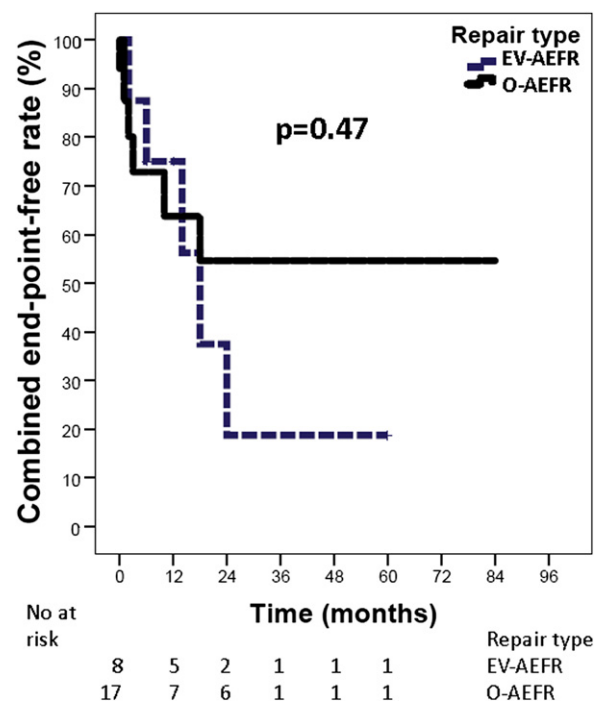
Table 5 Two-year event-free and survival rates in the two study groups.

| Two-year event rate | EV-AEFR | O-AEFR | p value |
|-----------------------------|---------|--------|---------|
| Recurrence-free rate | 51% | 78% | 0.58 |
| Sepsis-free rate | 28% | 70% | 0.22 |
| Reoperation-free rate | 30% | 64% | 0.58 |
| AEF-related death-free rate | 17% | 38% | 0.59 |
| Overall survival rate | 15% | 38% | 0.92 |

statistical significance (Table 5, Figs. 1–6). The early survival advantage of EV-AEFR was lost by the second year of follow-up (Fig. 5).

Recurrent AEF was developed in four patients. Two of them, where recurrence occurred after EV-AEFR and repeat EV-AEFR was performed (unsuccessfully in one of them), were eventually managed (due to repeat bleeding and sepsis, respectively) with conversion to conventional O-AEFR (graft removal and axillobifemoral bypass grafting). The two remaining patients, who originally had EV-AEFR and O-AEFR, respectively, were managed with graft removal/axillobifemoral bypass grafting and repeat aortic stump ligation; thus, 75% of all recurrent AEFs were in patients who had undergone EV-AEFR and this accounted for 3/8 (38%) of the total number of EV-AEFRs performed.

Recurrent or new-onset sepsis developed in six patients, in four of them after EV-AEFR. Management included conservative measures (antibiotics) in five patients (three of them succumbed, and two had subsequent graft removal/axillobifemoral bypass grafting) and graft removal/axillobifemoral bypass grafting in the last one. Two above-knee amputations, one in each study group, were performed during long-term follow-up, and an additional patient of the O-AEFR developed graft thrombosis. In summary, four patients (50%) of the EV-AEFR group (three

**Figure 1** AEF recurrence-free rates of the EV-AEFR and O-AEFR study groups were equivalent.**Figure 2** Sepsis-free rates of the EV-AEFR and O-AEFR study groups. A non significant trend for higher sepsis-free rates in O-AEFR compared to EV-AEFR was evident. Sepsis was defined as recurrent or new onset sepsis.**Figure 3** Freedom from the combined endpoint of AEF recurrence or development of sepsis (either new or recurrent) in the EV-AEFR and O-AEFR study groups was equivalent; a delay in the former group was noted.

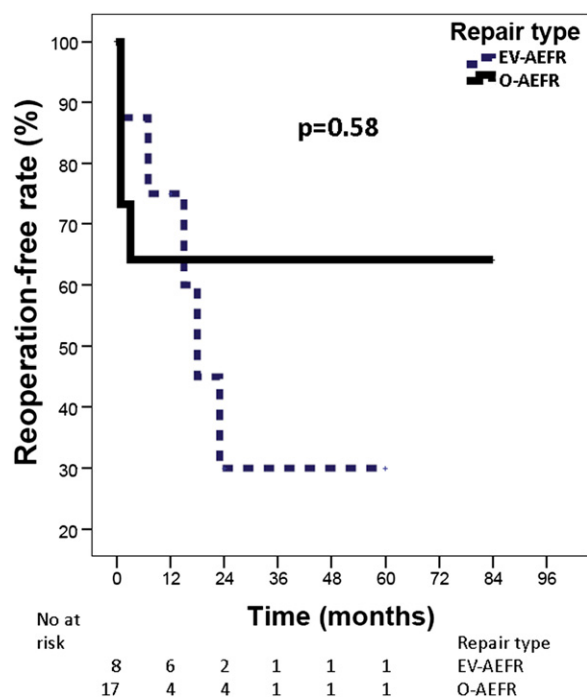


Figure 4 Re-operation-free rates of the EV-AEFR and O-AEFR study groups were equivalent, but the corresponding curves diverged around the 18th postoperative month, with higher rates being observed in the latter group.

due to sepsis, one due to recurrent AEF after a mean of 16.5 months, median 17.5 months) crossed over to the O-AEFR group with 100% mortality. An additional patient of the EV-AEFR group died after 2 years as a result of sepsis that was

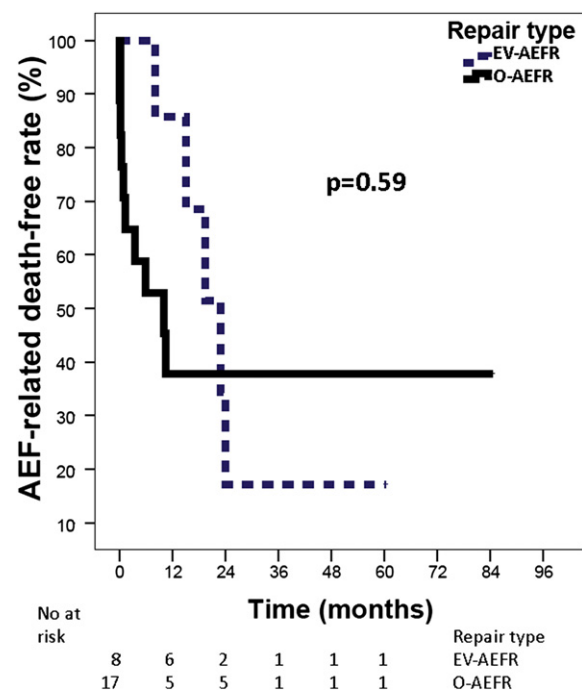


Figure 5 AEF-related death-free rates of the EV-AEFR and O-AEFR study groups were equivalent, but a delay in the former group was noted. The survival curves crossed at two years.

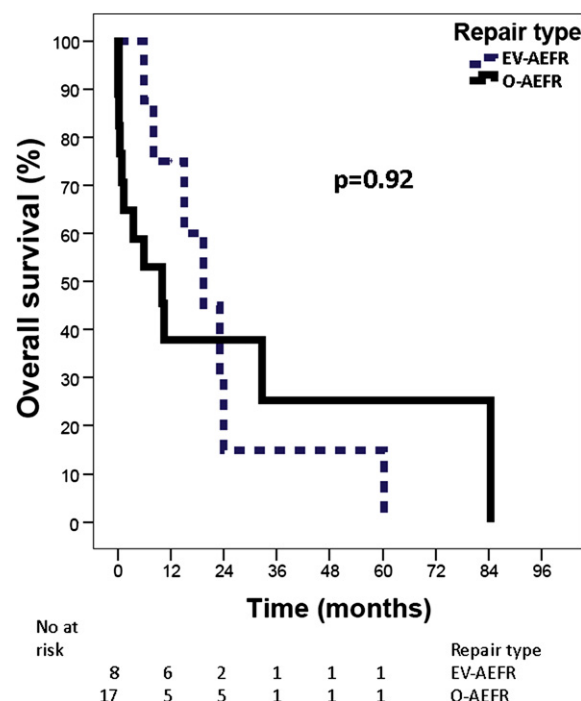


Figure 6 Overall death-free rates of the EV-AEFR and O-AEFR study groups were equivalent, but a delay in the former group was noted. The survival curves crossed toward the end of the second postoperative year.

managed conservatively, with two more dying because of a myocardial infarction at 6 months and 5 years, respectively. Of the 11 patients of the O-AEFR group, who were discharged alive, two patients died as a result of recurrent bleeding at 3 and 6 months, respectively, one patient after 10 months as a result of sepsis that was managed conservatively, two patients after an above-knee amputation (with co-current AEF-related sepsis) and cardiac surgery, at 11 and 84 months, respectively and one patient as a result of an myocardial infarction at 33 months. A flowchart summarising procedures and outcomes in relation to the study group is shown in Fig. 7.

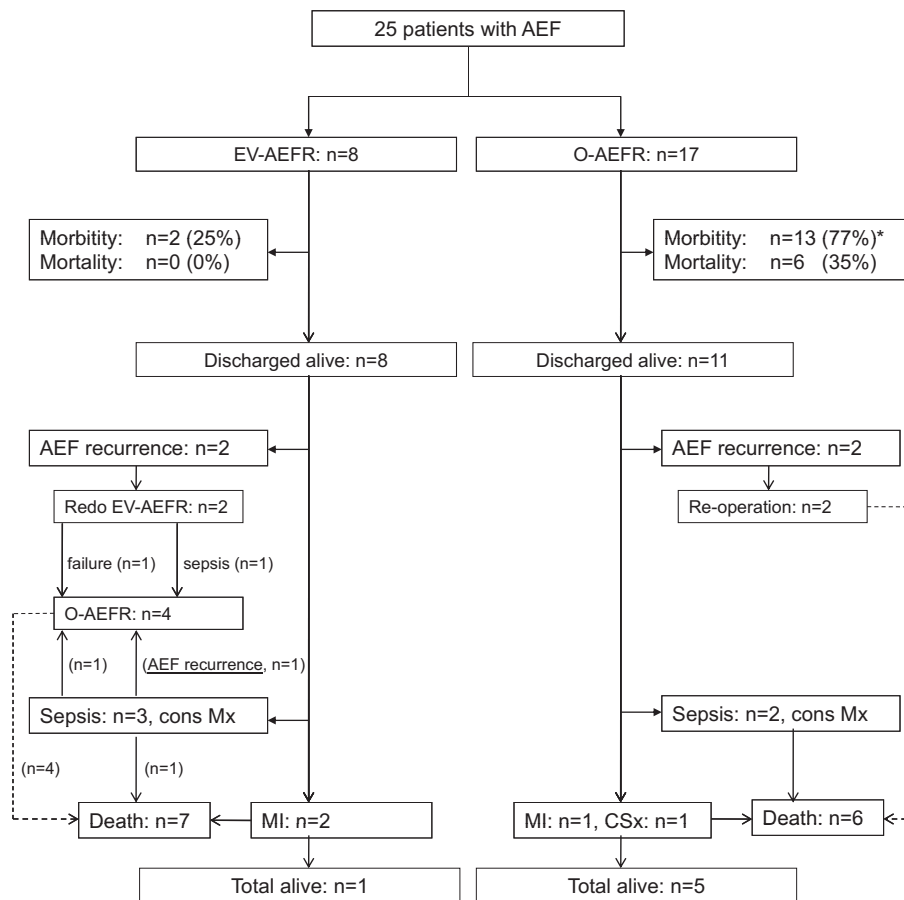
Factors affecting long-term outcome

Factors affecting recurrence rates

Preoperative sepsis had no effect on recurrence-free rates ($p = 0.94$) and so the remaining clinical characteristics on univariate or multivariate analysis.

Factors affecting new onset or recurrence of sepsis

There was a lower sepsis-free rate at 2 years in patients receiving two antibiotics after discharge (0%) compared with those who received only one antibiotic (63%) or no antibiotics (100%, p for trend = 0.006). There was a lower sepsis-free rate at 2 years in patients receiving antibiotics for longer than 6 months (22%) compared with those who received antibiotics for 6 months or less (83%, $p = 0.02$). Preoperative sepsis had no effect on sepsis-free rates ($p = 0.92$) and so the remaining clinical characteristics on univariate or multivariate analysis.



*recurrent bleeding (n=1), cons Mx: conservative management, CSx: cardiac surgery

Figure 7 Flow chart summarizing procedures and outcomes in relation to study group.

Factors affecting the combined endpoint of AEF recurrence or new-onset/recurrence of sepsis

There was a lower combined event-free rate at 2 years in patients whose original repair was AAA repair (18%) compared with those who had aortobifemoral bypass grafting (89%, $p = 0.02$).

There was a lower combined event-free rate at 2 years in patients, who had complex bowel repair (bowel resection with primary anastomosis or duodenal closure) (26%), compared with simple primary repair (83%, $p = 0.018$). No other associations were found on univariate or multivariate analysis.

Factors affecting re-operation rates

There was a lower re-operation-free rate at 10 months in patients, who had duodenal closure (17%), compared with simple primary repair (87%, $p = 0.012$). No other associations were found. On multivariate analysis, the number of symptoms (two vs. one) at presentation was the single predictor of re-operation ($p = 0.04$, relative risk 5.8, 95% C.I. 1.1–31).

Factors affecting AEF-related death

There was a worse AEF-related survival at 2 years in patients whose original repair was AAA repair (8%) compared with those who had aortobifemoral bypass

grafting (78%, $p = 0.013$). Patients, who had O-AEFR and their graft was not removed during this index operation ($n = 4$), had worse AEF-related 2-year survival compared with the remaining patients of both groups (0% vs. 39%, $p < 0.001$). No other associations were found. On multivariate analysis, the number of symptoms (two vs. one) at presentation was the single predictor of worse survival ($p = 0.018$, relative risk 13.8, 95% C.I. 1.6–123).

Factors affecting overall survival

There was a worse survival at 2 years in patients who presented with fever (11%) compared with those without fever (52%, $p = 0.04$). Two-year overall survival in patients with preoperative sepsis was worse (24%) compared with those without such presentation (50%, $p = 0.32$, Fig. 8). There was a worse survival at 2 years in patients whose original repair was AAA repair (8%), compared with those who had aortobifemoral bypass grafting (50%, $p = 0.035$). Patients, who had O-AEFR and their graft was not removed during this index operation ($n = 4$), had worse overall 2-year survival compared with the remaining patients of both groups (0% vs. 37%, $p = 0.001$). There was a worse survival at 2 years in patients receiving antibiotics for longer than 6 months (0%) compared with those who received antibiotics for 6 months or less (67%, $p = 0.03$). No other associations were found. On

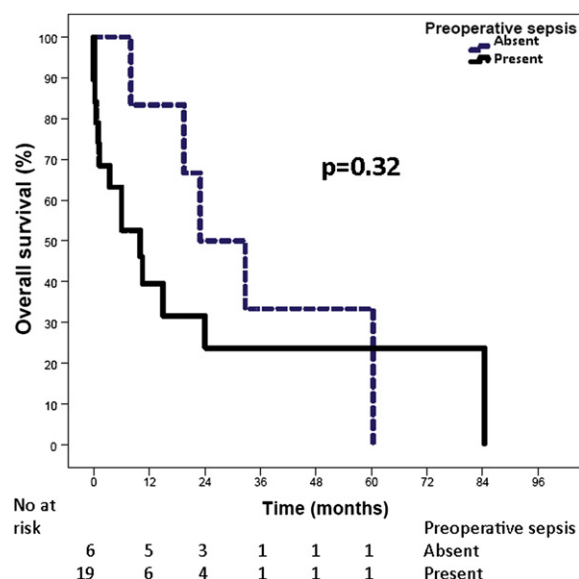


Figure 8 Preoperative sepsis was associated with worse two-year overall survival (24% vs 50%) but the difference did not reach statistical significance ($p = 0.32$).

multivariate analysis, the number of symptoms (two vs. one) at presentation was the single predictor of worse survival ($p = 0.012$, relative risk 17.8, 95% C.I. 1.8–135).

Discussion

In the present investigation, we reported on a multicentre study comparing EV-AEFR with O-AEFR. Despite not being a randomised study, the two study groups were comparable, although there was a strong trend for patients in the EV-AEFR group to have less often signs of infection preoperatively, indicating that bleeding dominated the clinical picture. AEF variety and the intestine segment involved were comparable with what previously reported,¹ although preoperative infection occurred more often in our study.

The main advantages of EV-AEFR are the low morbidity, mortality and associated hospitalisation, considerably less than O-AEFR. EV-AEFR is a less invasive method, does not require cross-clamping and thus is associated with less reperfusion injury and therefore is better tolerated in

patients, who are often debilitated and elderly, with bleeding and sepsis. Although minimally invasive, EV-AEFR has been reported to have some morbidity and mortality,^{6,8} most likely the result of haemodynamic instability and infection in a group of mostly elderly patients. However, these figures compare favourably with the outcome of O-AEFR, both in our series and the literature.^{1,6} Of note, mortality (35%) and morbidity (77%) after O-AEFR in our study were similar to what reported by others.^{1,11} Multiple organ failure was a particularly frequent complication after O-AEFR, with limb ischaemia, observed also by others,¹² being equally frequent. Mortality was worse in patients, who did not have graft removal, compared with the remainder, as expected; perioperative mortality with this type of management has been reported to be higher compared with more radical procedures,¹ a fact that favours the radical procedures in fit patients. In addition, certain trends were observed for preoperative sepsis and simple bowel repair which were associated with worse short-term outcomes, consistent with previous studies.^{11,13} As simple bowel repair has been associated with fatal leak,¹¹ we favour an aggressive management of the intestinal defect and suggest further study of complex duodenum closure, observed to be associated by others with worse outcome.¹³ Compared with elective EVAR, hospitalisation after O-AEFR in our series is significantly longer; this might partially reflect the need for intravenous antibiotics, especially to treat patients with persistent sepsis. Nevertheless, in our series, O-AEFR was associated with longer hospitalisation compared with EV-AEFR; similar results have been previously reported.⁶

Long-term complications after EV-AEFR and O-AEFR were equally encountered in our study; although O-AEFR is supposed to be a “permanent” solution, it is however plagued by a high rate of recurrent bleeding (aortic stump related) and septic complications. In the short term, recurrent bleeding and re-operation free rates are in favour of EV-AEFR, while, in the long term, bleeding and sepsis-free rates are better after O-AEFR (Figs. 1 and 2); our finding of a high incidence of recurrent or new onset of sepsis after EV-AEFR is consistent with previous reports.^{4,8,14} Similarly, recurrent bleeding after EV-AEFR has been reported to occur very often.¹⁵ However, the small number of patients (especially in the EV-AEFR) did not permit statistical significance, representing most likely a type II statistical error. More importantly, disease-related and overall survival were consistently better for the EV-AEFR group, a difference that persisted up to 24 months postoperatively, until the late mortality rate associated with graft removal offset the early survival benefit due to the absence of postoperative mortality. It should be noted that patients with AEFs have limited overall survival,⁶ and 2-year survival rates after O-AEFR average 30%,¹⁶ figuring similar to our results.

In our study, patients whose original repair was AAA repair developed recurrence and/or sepsis during follow-up more often, compared with those who had had aortobifemoral bypass grafting as also worse survival rates. The reason for this complicated course is unclear and could be related to the presence of the aneurysm sac, left in place after AAA repair, which could make infection eradication more difficult; the latter is likely associated with worse outcome in infected aneurysms.^{17,18} Similarly, prognosis was worse for patients,

Table 6 Lessons learnt from the current study.

- EV-AEFR has lower morbidity, compared to O-AEFR.
- EV-AEFR has no mortality, compared to O-AEFR, where only 2/3 of patients were discharged alive.
- Recurrence-free and sepsis-free rates of the two treatment methods were similar.
- Due to sepsis and/or recurrent AEF, the early survival advantage of EV-AEFR was lost after two years and overall long-term survival rates were similar.
- Bleeding and fever on presentation are poor prognostic features.
- Future trials should focus on the role of EV-AEFR, a) in patients at high risk for O-AEFR (due to shock or co-morbidities) or b) as a bridging procedure.

who had complex bowel repair, compared with simple primary repair, a result most likely of worse local sepsis. Simple primary repair was also associated with fewer re-operations. Sepsis-free rates were worse in patients receiving one or two antibiotics after discharge, especially if these were taken for longer than 6 months. We believe that this finding might be related to the fact that antibiotics are routinely prescribed for a prolonged period in patients after EV-AEFR, compared with selective use after O-AEFR,¹⁹ and to the fact that the former develop recurrent or new sepsis more often. Of note, survival was worse in patients who presented with fever. Finally, on multivariate analysis, complex presentation (mostly bleeding with fever) was associated with a worse survival outcome compared with patients presenting with a single symptom. Sepsis is known to be associated with worse patient survival after EV-AEFR,²⁰ and perhaps the combination with bleeding aggravates its prognostic role. AEF-related and overall survival in those patients, who did not have graft removal, was significantly worse compared with the remainder, findings related to the worse perioperative mortality associated with this type of management.¹

The long-term complications after EV-AEFR indicate that this method should preferentially serve as a bridge to open repair (O-AEFR) while patients are haemodynamically stabilised, local and systemic sepsis is managed and co-morbidities are worked up. This process of improving patient fitness and excluding those who are not good candidates could theoretically improve the results of O-AEFR, in both the short- and long-term, the latter being historically dismal.¹⁶ Alternatively, fit patients who had EV-AEFR could be followed-up closely until complications arise and have O-AEFR on an urgent or semi-elective basis. Study limitations include its non-randomised design and the relatively small number of patients, especially in the EV-AEFR group. Longer follow-up in a larger set of patients could yield additional observations and identify subgroups in which EV-AEFR is not associated with long-term complications, such as sepsis or AEF recurrence. Future work should be directed towards clarifying these questions. Having said that, the rarity, fortunately, of AEF, in the era of declining open aortic procedures, makes very difficult the design of a randomised study comparing EV-AEFR with O-AEFR. *In situ* O-AEFR with homografts, shown to achieve promising short- and long-term results, superior to conventional methods in one study,²¹ but inferior in another,²² deserves further research. A summary of the lessons learnt from the current study is shown in Table 6.

In conclusion, EV-AEFR was shown to have fewer complications and lower mortality, but this short-term advantage was lost during the second postprocedural year, which indicates that EV-AEFR should serve as a bridging option in selected patients. Further trials should focus on the role of EV-AEFR in patients at high risk for O-AEFR, due to shock or co-morbidities, or as a bridge therapy, and investigate methods to eliminate sepsis in an effort to improve patient survival.

Conflict of Interest/Funding

None.

References

- 1 Bergqvist D, Bjorck M. Secondary arterioenteric fistulation – a systematic literature analysis. *Eur J Vasc Endovasc Surg* 2009; **37**:31–42.
- 2 Deshpande A, Lovelock M, Mossop P, Denton M, Vidovich J, Gurry J. Endovascular repair of an aortoenteric fistula in a high-risk patient. *J Endovasc Surg* 1999; **6**:379–84.
- 3 Burks JA, Faries PL, Gravereaux EC, Hollier LH, Marin ML. Endovascular repair of bleeding aortoenteric fistulas: a 5-year experience. *J Vasc Surg* 2001; **34**:1055–9.
- 4 Chuter TAM, Lukaszewicz GC, Reilly LM, Kerlan RK, Faruqi R, Sawhney R, et al. Endovascular repair of a presumed aortoenteric fistula: late failure due to recurrent infection. *J Endovasc Ther* 2000; **7**:240–4.
- 5 Eskandari MK, Makaroun MS, Abu-Elmagd KM, Billiar TR. Endovascular repair of an aortoduodenal fistula. *J Endovasc Ther* 2000; **7**:328–32.
- 6 Baril DT, Carroccio A, Ellozy SH, Palchik E, Sachdev U, Jacobs TS, et al. Evolving strategies for the treatment of aortoenteric fistulas. *J Vasc Surg* 2006; **44**:250–7.
- 7 Kotsis T, Lioupis C, Tzanis A, Nasiopoulou P, Goumas K, Bakoyiannis K, et al. Endovascular repair of a bleeding secondary aortoenteric fistula with acute leg ischemia: a case report and review of the literature. *J Vasc Interv Radiol* 2006; **17**:563–7.
- 8 Danneels ML, Verhagen HJM, Teijink JAW, Cuypers P, Nevelsteen A, Vermassen FEG. Endovascular repair for aortoenteric fistula: a bridge too far or a bridge to surgery? *Eur J Vasc Endovasc Surg* 2006; **32**:27–33.
- 9 Antoniadis P, Geropapas G, Kounougeri E, Stamos D, Kalamaras A, Dervisis K. Acutely bleeding aortoduodenal fistula: staged endovascular and open surgical repair. *Vascular* 2009; **17**:197–200.
- 10 Kakkos SK, Christeas N, Lampropoulos G, Papadoulas S, Makri R, Zambakis P, et al. Endovascular management of aortoenteric fistulas with aortic cuff extenders: report of two cases. *Int Angiol* 2010, in press.
- 11 Valentine RJ, Timaran CH, Modrall GJ, Smith ST, Arko FR, Clagett GP. Secondary aortoenteric fistulas versus paraprosthetic erosions: is bleeding associated with a worse outcome? *J Am Coll Surg* 2008; **207**:922–7.
- 12 Reilly LM, Altman H, Lusby RJ, Kersh RA, Ehrenfeld WK, Stoney RJ. Late results following surgical management of vascular graft infection. *J Vasc Surg* 1984; **1**:36–44.
- 13 Cendan JC, Thomas IV JB, Seeger JM. Twenty-one cases of aortoenteric fistula: lessons for the general surgeon. *Am Surg* 2004; **70**:583–7.
- 14 El Sakka K, Halawa M, Kotze C, Francis I, Doyle T, Yusuf W. Complications of open abdominal aortic surgery: the endovascular solution. *Interact CardioVasc Thorac Surg* 2008; **7**:121–5.
- 15 Leonhardt H, Mellander S, Snygg J, Loenn L. Endovascular management of acute bleeding arterioenteric fistulas. *Cardiovasc Intervent Radiol* 2008; **31**:542–9.
- 16 O'Hara PJ, Hertzner NR, Beven EG, Krajewski LP. Surgical management of infected abdominal aortic grafts: review of a 25-year experience. *J Vasc Surg* 1986; **3**:725–31.
- 17 Satta J, Immonen K, Reinila A, Pokela R, Juvonen T. Outcome of elective infrarenal abdominal aortic aneurysm repair—an analysis of 174 consecutive patients. *Ann Chir Gynaecol* 1996; **85**:231–5.
- 18 Sriussadaporn S. Infected abdominal aortic aneurysms. Experience with 14 consecutive cases. *Int Surg* 1996; **81**:395–9.
- 19 Malone JM, Lalka SG, McIntyre KE, Bernhard VM, Pabst TS. The necessity for long-term antibiotic therapy with positive arterial wall cultures. *J Vasc Surg* 1988; **8**:262–7.

- 20 Antoniou GA, Koutsias S, Antoniou S, Georgiakakis A, Lazarides M, Giannoukas AD. Outcome after endovascular stent graft repair of aortoenteric fistula: a systematic review. *J Vasc Surg* 2009;**49**:782–9.
- 21 Bisdas T, Bredt M, Pichlmaier M, Aper T, Wilhelmi M, Bisdas S, et al. Eight-year experience with cryopreserved arterial homografts for the in situ reconstruction of abdominal aortic infections. *J Vasc Surg* 2010;**52**:323–30.
- 22 Lavigne JP, Postal A, Kolh P, Limet R. Prosthetic vascular infection complicated or not by aortoenteric fistula: comparison of treatment with and without cryopreserved allograft (homograft). *Eur J Vasc Endovasc Surg* 2003;**25**:416–23.